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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	**PAPER NUMBER**
1656	

DATE MAILED: 03/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/690,949	KATZ ET AL.	
	Examiner	Art Unit	
	William W. Moore	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2004*.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claim 11 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel claim 11, or amend claim 11 to place the claim in proper dependent form. While both claims are included in the following restriction requirement, claim 11 is objected to for describing subject matter identical to that stated in claim 10 from which it depends.

Restriction

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

1. Claims 6 and 18 drawn in part to, and claims 1, 16 and 19 drawn particularly to, a *Streptomyces hygroscopicus* host cell producing the compound 16-desmethyl-27-desmethoxyrapamycin and to a method of use of the cell in producing the compound, classified in class 435, subclass 252.35.
2. Claims 2 and 20, drawn to the compound 16-desmethyl-27-desmethoxyrapamycin, classified in class 415, subclass 33.
3. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,18-dihydrorapamycin, classified in class 435, subclass 252.35.
4. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 19,20-dihydrorapamycin, classified in class 435, subclass 252.35.
5. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 12,22-dihydrorapamycin, classified in class 435, subclass 252.35.
6. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,18,19,20-tetrahydrorapamycin, classified in class 435, subclass 252.35.
7. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,18,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.
8. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 19,20,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.
9. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,18,19,20,21,22-hexahydrorapamycin, classified in class 435, subclass 252.35.
10. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 16-demethyl-17,18-dihydrorapamycin, classified in class 435, subclass 252.35.

11. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 16-demethyl-19,20-dihydrorapamycin, classified in class 435, subclass 252.35.
12. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 16-demethyl-21,22-dihydrorapamycin, classified in class 435, subclass 252.35.
13. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 16-demethyl-17,18,19,20-tetrahydrorapamycin, classified in class 435, subclass 252.35.
14. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 16-desmethyl-17,18,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.
15. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 16-demethyl-19,20,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.
16. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 16-demethyl-17,18,19,20,21,22-hexahydrorapamycin, classified in class 435, subclass 252.35.
17. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17-desmethylrapamycin, classified in class 435, subclass 252.35.
18. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 23-desmethylrapamycin, classified in class 435, subclass 252.35.
19. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,23-didesmethylrapamycin, classified in class 435, subclass 252.35.
20. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17-desmethyl-17,18-dihydrorapamycin, classified in class 435, subclass 252.35.
21. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17-desmethyl-19,20-dihydrorapamycin, classified in class 435, subclass 252.35.
22. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17-desmethyl-21,22-dihydrorapamycin, classified in class 435, subclass 252.35.
23. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17-desmethyl-17,18,19,20-tetrahydrorapamycin, classified in class 435, subclass 252.35.
24. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17-desmethyl-17,18,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.
25. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17-desmethyl-19,20,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.

26. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17-desmethyl-17,18,19,20,21,22-hexahydrorapamycin,

27. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 23-desmethyl-17,18-dihydrorapamycin, classified in class 435, subclass 252.35.

28. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 23-desmethyl-19,20-dihydrorapamycin, classified in class 435, subclass 252.35.

29. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 23-desmethyl-21,22-dihydrorapamycin, classified in class 435, subclass 252.35.

30. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 23-desmethyl-17,18,19,20-tetrahydrorapamycin, classified in class 435, subclass 252.35.

31. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 23-desmethyl-17,18,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.

32. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 23-desmethyl-19,20,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.

33. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 23-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, classified in class 435, subclass 252.35.

34. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,23-didesmethyl-17,18-dihydrorapamycin, classified in class 435, subclass 252.35.

35. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,23-didesmethyl-19,20-dihydrorapamycin, classified in class 435, subclass 252.35.

36. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,23-didesmethyl-21,22-dihydrorapamycin, classified in class 435, subclass 252.35.

37. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,23-didesmethyl-17,18,19,20-tetrahydrorapamycin, classified in class 435, subclass 252.35.

38. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,23-didesmethyl-17,18,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.

39. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,23-didesmethyl-19,20,21,22-tetrahydrorapamycin, classified in class 435, subclass 252.35.

40. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 17,23-didesmethyl-17,18,19,20,21,22-hexahydrorapamycin, classified in class 435, subclass 252.35.

41. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 19-methylrapamycin, classified in class 435, subclass 252.35.
42. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 19,20-del-rapamycin, classified in class 435, subclass 252.35.
43. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 18-hydroxyrapamycin, classified in class 435, subclass 252.35.
44. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 18-ketorapamycin, classified in class 435, subclass 252.35.
45. Claim 3, drawn in part to a *Streptomyces hygroscopicus* host cell producing the compound 18-saturated-rapamycin, classified in class 435, subclass 252.35.
46. Claim 4, drawn in part to the compound 17,18-dihydrorapamycin, classified in class 415, subclass 33.
47. Claim 4, drawn in part to the compound 19,20-dihydrorapamycin, classified in class 415, subclass 33.
48. Claim 4, drawn in part to the compound 12,22-dihydrorapamycin, classified in class 415, subclass 33.
49. Claim 4, drawn in part to the compound 17,18,19,20-tetrahydrorapamycin, classified in class 415, subclass 33.
50. Claim 4, drawn in part to the compound 17,18,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.
51. Claim 4, drawn in part to the compound 19,20,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.
52. Claim 4, drawn in part to the compound 17,18,19,20,21,22-hexahydrorapamycin, classified in class 415, subclass 33.
53. Claim 4, drawn in part to the compound 16-demethyl-17,18-dihydrorapamycin, classified in class 415, subclass 33.
54. Claim 4, drawn in part to the compound 16-demethyl-19,20-dihydrorapamycin, classified in class 415, subclass 33.
55. Claim 4, drawn in part to the compound 16-demethyl-21,22-dihydrorapamycin, classified in class 415, subclass 33.
56. Claim 4, drawn in part to the compound 16-demethyl-17,18,19,20-tetrahydrorapamycin, classified in class 415, subclass 33.
57. Claim 4, drawn in part to the compound 16-demethyl-17,18,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.
58. Claim 4, drawn in part to the compound 16-demethyl-19,20,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.
59. Claim 4, drawn in part to the compound 16-demethyl-17,18,19,20,21,22-hexahydrorapamycin, classified in class 415, subclass 33.
60. Claim 4, drawn in part to the compound 17-desmethylrapamycin, classified in class 415, subclass 33.

61. Claim 4, drawn in part to the compound 23-desmethylrapamycin, classified in class 415, subclass 33.
62. Claim 4, drawn in part to the compound 17,23-didesmethylrapamycin, classified in class 415, subclass 33.
63. Claim 4, drawn in part to the compound 17-desmethyl-17,18-dihydrorapamycin, classified in class 415, subclass 33.
64. Claim 4, drawn in part to the compound 17-desmethyl-19,20-dihydrorapamycin, classified in class 415, subclass 33.
65. Claim 4, drawn in part to the compound 17-desmethyl-21,22-dihydrorapamycin, classified in class 415, subclass 33.
66. Claim 4, drawn in part to the compound 17-desmethyl-17,18,19,20-tetrahydrorapamycin, classified in class 415, subclass 33.
67. Claim 4, drawn in part to the compound 17-desmethyl-17,18,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.
68. Claim 4, drawn in part to the compound 17-desmethyl-19,20,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.
69. Claim 4, drawn in part to the compound 17-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, classified in class 415, subclass 33.
70. Claim 4, drawn in part to the compound 23-desmethyl-17,18-dihydrorapamycin, classified in class 415, subclass 33.
71. Claim 4, drawn in part to the compound 23-desmethyl-19,20-dihydrorapamycin, classified in class 415, subclass 33.
72. Claim 4, drawn in part to the compound 23-desmethyl-21,22-dihydrorapamycin, classified in class 415, subclass 33.
73. Claim 4, drawn in part to the compound 23-desmethyl-17,18,19,20-tetrahydrorapamycin, classified in class 415, subclass 33.
74. Claim 4, drawn in part to the compound 23-desmethyl-17,18,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.
75. Claim 4, drawn in part to the compound 23-desmethyl-19,20,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.
76. Claim 4, drawn in part to the compound 23-desmethyl-17,18,19,20,21,22-hexahydrorapamycin, classified in class 415, subclass 33.
77. Claim 4, drawn in part to the compound 17,23-didesmethyl-17,18-dihydrorapamycin, classified in class 415, subclass 33.
78. Claim 4, drawn in part to the compound 17,23-didesmethyl-19,20-dihydrorapamycin, classified in class 415, subclass 33.
79. Claim 4, drawn in part to the compound 17,23-didesmethyl-21,22-dihydrorapamycin, classified in class 415, subclass 33.
80. Claim 4, drawn in part to the compound 17,23-didesmethyl-17,18,19,20-tetrahydrorapamycin, classified in class 415, subclass 33.

81. Claim 4, drawn in part to the compound 17,23-didesmethyl-17,18,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.

82. Claim 4, drawn in part to the compound 17,23-didesmethyl-19,20,21,22-tetrahydrorapamycin, classified in class 415, subclass 33.

83. Claim 4, drawn in part to the compound 17,23-didesmethyl-17,18,19,20,21,22-hexahydrorapamycin, classified in class 415, subclass 33.

84. Claim 4, drawn in part to the compound 19-methylrapamycin, classified in class 415, subclass 33.

85. Claim 4, drawn in part to the compound 19,20-del-rapamycin, classified in class 415, subclass 33.

86. Claim 4, drawn in part to the compound 18-hydroxyrapamycin, classified in class 415, subclass 33.

87. Claim 4, drawn in part to the compound 18-ketorapamycin, classified in class 415, subclass 33.

88. Claim 4, drawn in part to the compound 18-saturated-rapamycin, classified in class 415, subclass 33.

89. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 1 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

90. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active dehydratase domain of module 1 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

91. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active enoylreductase domain of module 1 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

92. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active extender domain of module 2 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

93. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 3 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

94. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active dehydratase domain of module 3 and that further comprises either a portion of a heterologous polyketide synthase or an

inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

95. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active enoylreductase domain of module 3 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

96. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 4 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

97. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active dehydratase domain of module 4 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

98. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 5 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

99. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active dehydratase domain of module 6 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

100. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 7 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

101. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active dehydratase domain of module 7 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

102. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active enoylreductase domain of module 7 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

103. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 8 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

104. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active dehydratase domain of module 8 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

105. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 9 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

106. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active dehydratase domain of module 9 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

107. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 10 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

108. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active dehydratase domain of module 10 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

109. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 11 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

110. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 12 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

111. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active ketoreductase domain of module 13 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

112. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that comprises an active dehydratase domain of module 13 and further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435 or an inactivated domain of a rapamycin polyketide synthase module, subclass 69.7.

113. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active enoylreductase domain of module 13 and that further

comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

114. Claims 5 and 17, drawn in part to a *Streptomyces hygroscopicus* host cell that expresses an active extender domain of module 14 and that further comprises either a portion of a heterologous polyketide synthase or an inactivated domain of a rapamycin polyketide synthase module, classified in class 435, subclass 69.7.

115. Claims 6-9 drawn in part to, and claims 10 and 11 more particularly drawn to a *Streptomyces hygroscopicus* host cell comprising a polynucleotide encoding the *rap*N P450 hydroxylase and expressing the hydroxylase but incapable of expressing another rapamycin modification enzyme, classified in class 435, subclass 471.

116. Claims 6-9 drawn in part to, and claims 10 and 11 more particularly drawn to a *Streptomyces hygroscopicus* host cell comprising a polynucleotide encoding the *rap*O ferredoxin and expressing the ferredoxin but incapable of expressing another rapamycin modification enzyme, classified in class 435, subclass 471.

117. Claims 6-9 drawn in part to, and claims 12-14 more particularly drawn to a *Streptomyces hygroscopicus* host cell comprising a polynucleotide encoding the *rap*I O-methyltransferase and expressing the O-methyltransferase but incapable of expressing another rapamycin modification enzyme, classified in class 435, subclass 471.

118. Claims 6-9 drawn in part to, and 12-15 claims more particularly drawn to a *Streptomyces hygroscopicus* host cell comprising a polynucleotide encoding the *rap*J P450 hydroxylase and expressing the hydroxylase but incapable of expressing another rapamycin modification enzyme, classified in class 435, subclass 471.

119. Claims 6-9 drawn in part to, and claim 12 more particularly drawn to a *Streptomyces hygroscopicus* host cell comprising a polynucleotide encoding the *rap*M O-methyltransferase and expressing the O-methyltransferase but incapable of expressing another rapamycin modification enzyme, classified in class 435, subclass 471.

120. Claims 6-9 drawn in part to, and claims 12 and 13 more particularly drawn to a *Streptomyces hygroscopicus* host cell comprising a polynucleotide encoding the *rap*Q O-methyltransferase and expressing the O-methyltransferase but incapable of expressing another rapamycin modification enzyme, classified in class 435, subclass 471.

The inventions are distinct, each from the other, because of the following reasons:

The invention of Group 1 is related to the invention of Group 2 as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In

the instant case the product as claimed can be used in a materially different process of using that product, making a modified polyketide synthase and ancillary rapamycin modification enzymes by recombinant expression thereof.

The invention of Group 1 is unrelated to the inventions of Groups 3-45. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different host cells comprise polynucleotides encoding differently-modified rapamycin synthases wherein each is required to produce different, specific, products, which host cells are not disclosed as capable of use together and comprise polynucleotides of different designs that have different effects.

The invention of Group 1 is unrelated to the inventions of Groups 46-88. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are a composition of matter, the host cell of Group 1, and forty-four structurally distinct chemical compounds of Groups 2 and 46-88 that are not disclosed as capable of use together and that have different designs, different modes of operation, and different effects.

The invention of Group 1 is unrelated to the inventions of Groups 89-114. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the different inventions are host cells that comprise polynucleotides encoding structurally distinct polyketide synthases wherein the host cell of Group 1 may not comprise a polynucleotide encoding a hybrid polyketide synthase while host cells of Groups 89-114 must all comprise polynucleotides encoding polyketide synthases comprising a component beyond any component of a rapamycin polyketide synthase, which host cells are not disclosed as capable of use together and have different effects.

The invention of Group 1 is unrelated to the inventions of Groups 115-120. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, host cells of the different Groups comprise polynucleotides encoding distinct sets of polyketide modification enzymes wherein the host cell of Group 1 need not, as claimed, comprise one or more modification enzymes

of host cells of Groups 115-120, which host cells are not disclosed as capable of use together and have different effects.

The invention of Group 2 is unrelated to the inventions of Groups 3-45. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the invention of Group 2 is a chemical compound and the inventions of Groups 3-45 compositions of matter, host cells, that, as claimed, need not comprise nor produce the compound of Group 2, which compound is not disclosed as capable of use together with the inventions of Groups 3-45 and has different effects.

The invention of Group 2 is unrelated to the inventions of Groups 46-88. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the invention of Group 2 is a chemical compound that is structurally distinct from the chemical compounds of Groups 46-88, which compounds are not disclosed as capable of use together and have different effects.

The invention of Group 2 is unrelated to the inventions of Groups 89-120. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the invention of Group 2 is a chemical compound and the inventions of Groups 89-114 are compositions of matter, host cells, that, as claimed, need not comprise or produce the compound of Group 2, which compound is not disclosed as capable of use together with the inventions of Groups 89-114 and has different effects.

The inventions of Groups 3-45 are unrelated, one to another. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inventions of Groups 3-45 are different host cells comprising different structural alterations of rapamycin polyketide synthase polypeptides not described the claims and that, as claimed, need not comprise or produce a product produced by another of Groups 3-45, and that are not disclosed as capable of use together and that each have different effects.

The inventions of Groups 3-45 are unrelated to the inventions of Groups 46-88. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inventions of Groups 3-45 are host cells, compositions of matter, that are distinct from the chemical compounds of Groups 46-88, which compositions of matter and which compounds are not disclosed as capable of use together and have different effects.

The inventions of Groups 3-45 are unrelated to the inventions of Groups 89-120. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inventions of Groups 3-45 are host cells that need not be related, as claimed, to any particular invention of the host cells of Groups 89-120, which host cells are not disclosed as capable of use together and have different effects.

The inventions of Groups 46-88 are unrelated, one to another. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inventions of Groups 46-88 are structurally distinct chemical compounds that are not disclosed as capable of use together and that each have different designs and different effects.

The inventions of Groups 46-88 are unrelated to the inventions of Groups 89-120. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inventions of Groups 3-45 are chemical compounds that are distinct from the host cells, compositions of matter, of Groups 89-120, and that need not be related, as claimed, to any particular invention of the host cells of Groups 89-120, nor are the compounds of Groups 89-120 disclosed as capable of use together with the host cells of Groups 89-120 and have different modes of operation and different effects.

The inventions of Groups 89-120 are unrelated, one to another. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case, the inventions of Groups 89-120 are host cells that

comprise polynucleotides encoding different kinds of modifications of rapamycin polyketide synthases or comprise polynucleotides encoding as few as one rapamycin polyketide modification enzyme yet need not be related, as claimed, to any particular other host cell of Groups 89-120, which host cells are not disclosed as capable of use together and have different effects.

Election

A telephone call was made to Mr. Randolph T. Apple on 2 March 2006 to request an oral election to the above restriction requirement, but did not result in an election being made. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee withdrawn required under 37 CFR 1.17(i).

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 571.272.0933 and whose FAX number is 571.273.0933. The examiner can normally be reached Monday through Friday between 9:00AM and 5:30PM EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisory Primary Examiner, Dr. Kathleen Kerr, can be reached at 571.272.0931. The official FAX number for all communications for the organization where this application or proceeding is assigned is 571.273.8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571.272.1600.

N-Shed
NASHAAT T. NASHED PHD.
PRIMARY EXAMINER

William W. Moore
2 March 2006